

in which:

$R^2$  to  $R^5$ , R and R' are as defined in formula I above; and

$R^{1b}$  is optionally substituted  $C_{1-6}$  alkyl, optionally substituted aryl, optionally substituted aryl acyl,  $C_{1-6}$  alkyl acyl or optionally substituted heterocyclyl.

5 Formula VIb represents compounds in which the 8-hydroxyl group on the quinoline is blocked to form a prodrug, in particular an ester prodrug. The 8-hydroxy represents a principal site of metabolism for the compound of Formula I: conjugation with glucuronic acid or sulphate gives a hydrophilic species ready to be excreted. Such conjugates probably do not pass the blood brain barrier. The ester prodrug may protect the compound of Formula I from  
10 conjugation. Esterases integral to the blood brain barrier may then release the C8-hydroxy on passage through that barrier activating the compound for its role in the CNS.

In a particularly preferred embodiment, the compound of formula I is a compound of formula Ib or IIb in which  $R^{4b}$  and  $R^{5b}$  or  $R^{4b'}$  and  $R^{5b'}$  are both halo, more preferably chloro substituents. Preferably, at least one of  $R^2$ , R,  $R^3$  and R' is optionally  
15 substituted alkyl, optionally substituted aryl, optionally substituted heterocyclyl,  $(CH_2)_nNR^9R^{10}$  in which  $R^9$  and  $R^{10}$  are as defined above and n is 1 to 4,  $COR^6$  in which  $R^6$  is  $NR^7R^8$ ,  $OR^7$  or  $SR^7$  in which  $R^7$  and  $R^8$  are as defined above or  $NR^{11}R^{12}$ ,  $OR^{11}$ ,  $SR^{11}$  in which  $R^{11}$  and  $R^{12}$  are as defined above.

While not wishing to be bound by theory, it is believed that substituents R,  $R^3$  and  
20 R' have a limited effect, electronically or sterically, in the chelating properties of the compounds of the present invention. Substitution at those positions can therefore be used to modulate other parameters such as cytotoxicity and physicochemical properties including the number of hydrogen bond donors and acceptors, lipophilicity (ClogP, ElogP and LogD), solubility and polar surface area. Modulation of these parameters contribute to the optimisation of the  
25 pharmacokinetic profile of the compounds. It is also postulated that substituent  $R^2$  in addition to modulating cytotoxicity and physicochemical properties could also affect activity if the substituent provides chelating properties. Examples of particularly preferred compounds having  $R^2$  substituents with chelating properties are shown below.

(m) when  $R^1$ ,  $R$ ,  $R^4$  and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R'$  is not 4-methoxyphenyl, 3-methylphenyl, pyridin-3-yl, benzyl, bromo, 4-chlorophenyl, 3,4-dichlorophenyl, 3-hydroxypropyl or 3-tert-butoxycarbonylaminopropyl;

(n) when  $R^1$ ,  $R$ ,  $R^4$  and  $R'$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R^5$  is not phenyl or 3-tert-butoxycarbonylaminoprop-1-yl;

(o) when  $R^1$ ,  $R$ ,  $R^4$ ,  $R'$  and  $R^5$  are H and  $R^2$  is  $\text{CO}_2\text{Me}$ , then  $R^3$  is not toluene-4-sulphonylamino, piperazin-1-yl, morpholin-1-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, 3-benzoylaminoprop-1-yl, phenethyl, 3-tert-butoxycarbonylaminopropyl, 3-hydroxypropyl, amino or hex-1-yl;

(p) when  $R^1$ ,  $R^4$ ,  $R'$  and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Na}$  and  $R^3$  is OH, then  $R$  is not phenyl;

(q) when  $R^1$ ,  $R$ ,  $R^4$ ,  $R'$  and  $R^5$  are H and  $R^2$  is  $\text{CO}_2\text{H}$ , then  $R^3$  is not phenyl, 4-chlorophenyl, phenethyl, 3-hydroxypropyl, amino, morpholin-1-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, toluene-4-sulphonylamino, 3-benzoylaminoprop-1-yl, aminoprop-1-ynyl, hex-1-yl, 5-hydroxypent-1-yl, piperazin-1-yl or 2-(1-piperazinyl)pyrimidinyl;

(r) when  $R^1$ ,  $R'$  and  $R$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R^4$  and  $R^5$  are not chloro;

(s) when  $R^1$ ,  $R^4$ ,  $R'$  and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R$  is not bromo;

(t) when  $R^1$ ,  $R'$  and  $R^4$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R$  and  $R^5$  are not bromo;

(u) when  $R^1$ ,  $R$ ,  $R^3$ ,  $R'$  and  $R^5$  are H and  $R^2$  is  $\text{CO}_2\text{H}$ , then  $R^4$  is not phenyl, 4-chlorophenyl or phenylethyl;

(v) when  $R^1$ ,  $R^5$ ,  $R'$ ,  $R^4$ ,  $R^3$  and  $R$  are H, then  $R^2$  is not 2H-tetrazol-1-yl;

(w) when  $R^1$ ,  $R^5$ ,  $R^4$  and  $R$  are H,  $R^2$  is  $\text{CO}_2\text{H}$  and  $R^3$  is OH, then  $R'$  is not 3,5-dichlorophenyl or 4-fluorophenyl; and

(x) at least one of  $R^1$  to  $R^5$ ,  $R$  and  $R'$  is other than H;

(y) when  $R^1$  to  $R^3$ ,  $R^5$ ,  $R'$  and  $R$  are H, then  $R^4$  is not chloro,  $\text{NH}_2$  or  $\text{SO}_3\text{H}$ ; and

(z) when  $R^1$ ,  $R^3$  to  $R^5$ ,  $R$  and  $R'$  are H, then  $R^2$  is not  $\text{CH}_3$ .

The compound of formula II defined above may be prepared using the processes described in detail hereinafter.

## DETAILED DESCRIPTION OF THE INVENTION

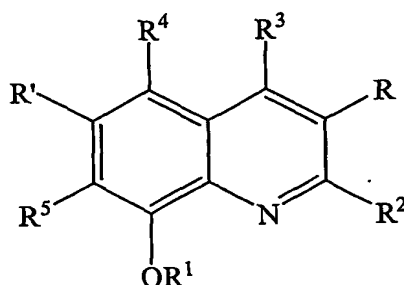
For the purposes of this specification it will be clearly understood that the word "comprising" means "including but not limited to", and that the word "comprises" has a corresponding meaning.

The term "alkyl" used either alone or in compound words such as "optionally substituted alkyl" "haloalkyl" or "alkyl acyl" refers to straight chain, branched chain or cyclic hydrocarbon groups having from 1 to 10 carbon atoms, preferably 1 to 6 carbon atoms, more

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method for the treatment, amelioration and/or prophylaxis of a neurological condition which comprises the administration of an effective amount of a compound of formula

I:



I

in which

$R^1$  is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted acyl, optionally substituted aryl, optionally substituted heterocyclyl, an antioxidant or a targeting moiety;

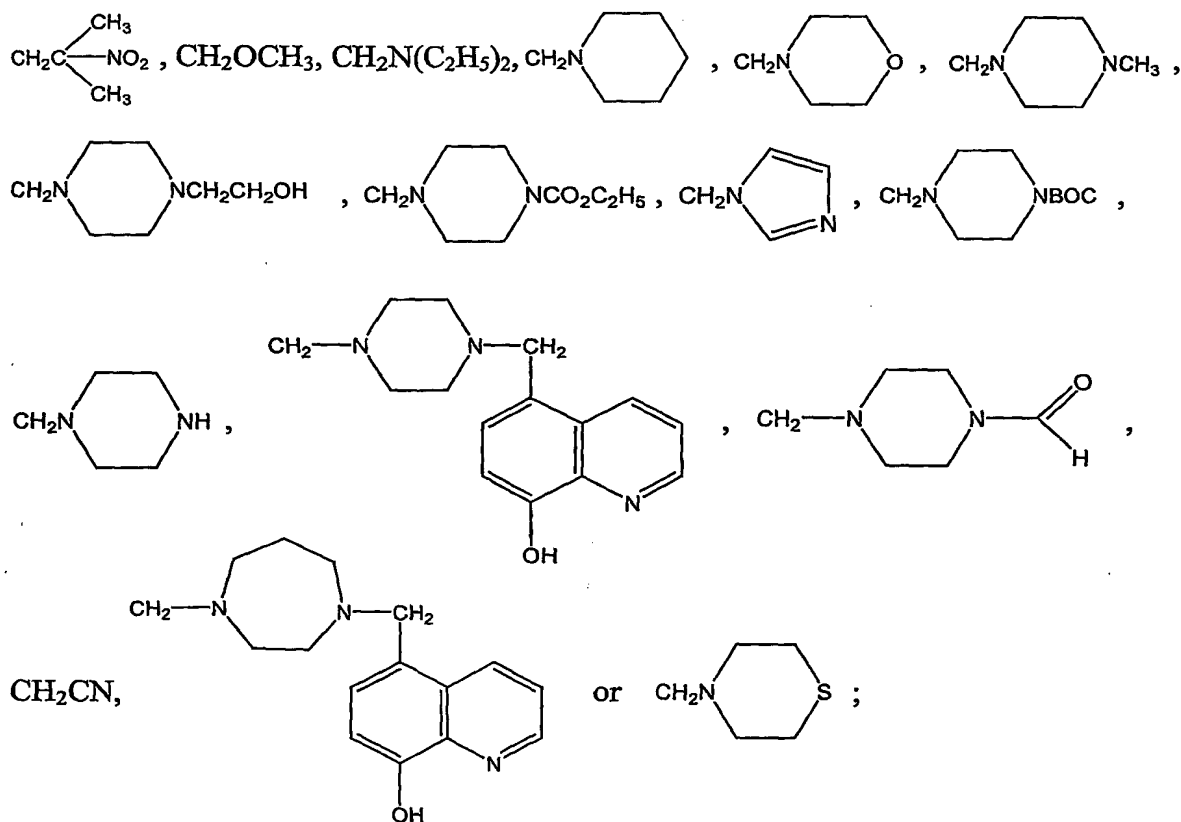
$R^2$  is H; optionally substituted alkyl; optionally substituted alkenyl; optionally substituted aryl; optionally substituted heterocyclyl; optionally substituted alkoxy; an antioxidant; a targeting moiety;  $COR^6$  or  $CSR^6$  in which  $R^6$  is H, optionally substituted alkyl, optionally substituted alkenyl, hydroxy, optionally substituted aryl, optionally substituted heterocyclyl, an antioxidant, a targeting moiety,  $OR^7$ ,  $SR^7$  or  $NR^7R^8$  in which  $R^7$  and  $R^8$  are either the same or different and selected from H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted aryl or optionally substituted heterocyclyl; CN;  $(CH_2)_nNR^9R^{10}$ ,  $HCONR^9$  or  $HCCNR^9R^{10}$  in which  $R^9$  and  $R^{10}$  are either the same or different and selected from H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted aryl or optionally substituted heterocyclyl and n is 1 to 4;  $OR^{11}$ ,  $SR^{11}$  or  $NR^{11}R^{12}$  in which  $R^{11}$  and  $R^{12}$  are either the same or different and selected from H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted aryl or optionally substituted heterocyclyl or together form optionally substituted heterocyclyl; or  $SO_2NR^{13}R^{14}$  in which  $R^{13}$  and  $R^{14}$  are either the same or different and selected from H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted aryl or optionally substituted heterocyclyl; and

$R^3$ ,  $R^4$ ,  $R^5$ , R and  $R'$  are either the same or different and selected from H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkoxy, optionally substituted acyl, hydroxy, optionally substituted amino, optionally substituted thio,

optionally substituted sulphonyl, optionally substituted sulphinyl, optionally substituted sulphonylamino, halo,  $\text{SO}_3\text{H}$ , amine, CN,  $\text{CF}_3$ , optionally substituted aryl, optionally substituted heterocyclyl, an antioxidant or a targeting moiety,

salts, hydrates, solvates, derivatives, pro-drugs, tautomers and/or isomers thereof with the provisos that:

- (a) when  $\text{R}^1$  to  $\text{R}^3$ , R and  $\text{R}'$  are H, then  $\text{R}^4$  is not Cl or I and  $\text{R}^5$  is not I;  
 (b) when  $\text{R}^1$  to  $\text{R}^3$ , R,  $\text{R}'$  and  $\text{R}^5$  are H, then  $\text{R}^4$  is not CHO,  $\text{CHOHCCl}_3$ ,



(c) when  $\text{R}^1$ ,  $\text{R}^5$ ,  $\text{R}'$  and R are H,  $\text{R}^2$  is  $\text{CO}_2\text{H}$  and  $\text{R}^3$  is OH, then  $\text{R}^4$  is not bromo, methyl, phenyl, hydroxymethyl or trifluoromethyl;

(d) when  $\text{R}^1$ ,  $\text{R}^4$ ,  $\text{R}^5$  and R are H,  $\text{R}^2$  is  $\text{CO}_2\text{H}$  and  $\text{R}^3$  is OH, then  $\text{R}'$  is not bromo, iodo, methyl, phenyl, propyl, phenethyl, heptyl, benzylaminomethyl, 3-aminopropyl, 3-hydroxypropyl, 4-methoxyphenyl, 3-methylphenyl, 4-chlorophenyl, 3,4-dichlorophenyl, pyridin-3-yl, furo-2-yl, 4-chlorophenyl, 3,4-dichlorophenyl, 2-chlorophenyl, 3-chlorophenyl, 2-chlorophenyl, 3-chlorophenyl, 2-methoxyphenyl or piperidin-2-yl;

(e) when  $\text{R}^1$ ,  $\text{R}^4$ , R and  $\text{R}'$  are H,  $\text{R}^2$  is  $\text{CO}_2\text{H}$  and  $\text{R}^3$  is OH, then  $\text{R}^5$  is not phenyl, 3-hydroxypropyl, phenethyl, 3-aminoprop-1-yl or hex-1-yl;

(f) when  $\text{R}^1$ ,  $\text{R}^4$ ,  $\text{R}'$  and  $\text{R}^5$  are H,  $\text{R}^2$  is  $\text{CO}_2\text{H}$  and  $\text{R}^3$  is OH, then R is not N-

morpholinomethyl, bromo or phenyl;

(g) when  $R^1$ , R and R' are H,  $R^2$  is  $\text{CO}_2\text{H}$  and  $R^3$  is OH, then  $R^4$  and  $R^5$  are not chloro;

(h) when  $R^1$ ,  $R^4$  and R' are H,  $R^2$  is  $\text{CO}_2\text{H}$  and  $R^3$  is OH, then R and  $R^5$  are not bromo;

(i) when  $R^1$ , R, R' and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R^4$  is not hydroxymethyl, phenyl or bromo;

(j) when  $R^1$ , R,  $R^4$  and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then R' is not 4-methoxyphenyl, 3-methylphenyl, pyridin-3-yl, benzyl, bromo, 4-chlorophenyl, 3,4-dichlorophenyl, 3-hydroxypropyl or 3-tert-butoxycarbonylaminopropyl;

(k) when  $R^1$ , R,  $R^4$  and R' are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R^5$  is not phenyl or 3-tert-butoxycarbonylaminoprop-1-yl;

(l) when  $R^1$ , R,  $R^4$ , R' and  $R^5$  are H and  $R^2$  is  $\text{CO}_2\text{Me}$ , then  $R^3$  is not toluene-4-sulphonylamino, piperazin-1-yl, morpholin-1-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, 3-benzoylaminoprop-1-yl, phenethyl, 3-tert-butoxycarbonylaminopropyl, 3-hydroxypropyl, amino or hex-1-yl;

(m) when  $R^1$ ,  $R^4$ , R' and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Na}$  and  $R^3$  is OH, then R is not phenyl;

(n) when  $R^1$ , R,  $R^4$ , R' and  $R^5$  are H and  $R^2$  is  $\text{CO}_2\text{H}$ , then  $R^3$  is not phenyl, 4-chlorophenyl, phenethyl, 3-hydroxypropyl, amino, morpholin-1-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, toluene-4-sulphonylamino, 3-benzoylaminoprop-1-yl, aminoprop-1-ynyl, hex-1-yl, 5-hydroxypent-1-yl, piperazin-1-yl or 2-(1-piperazinyl)pyrimidinyl;

(o) when  $R^1$ , R' and R are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R^4$  and  $R^5$  are not chloro;

(p) when  $R^1$ ,  $R^4$ , R' and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then R is not bromo;

(q) when  $R^1$ , R' and  $R^4$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then R and  $R^5$  are not bromo;

(r) when  $R^1$ , R,  $R^3$ , R' and  $R^5$  are H and  $R^2$  is  $\text{CO}_2\text{H}$ , then  $R^4$  is not phenyl, 4-chlorophenyl or phenylethyl;

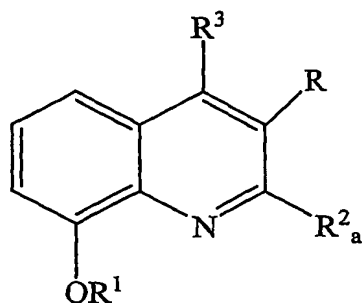
(s) when  $R^1$ ,  $R^5$ , R',  $R^4$ ,  $R^3$  and R are H, then  $R^2$  is not 2H-tetrazol-1-yl;

(t) when  $R^1$ ,  $R^5$ ,  $R^4$  and R are H,  $R^2$  is  $\text{CO}_2\text{H}$  and  $R^3$  is OH, then R' is not 3,5-dichlorophenyl or 4-fluorophenyl; and

(u) at least one of  $R^1$  to  $R^5$ , R and R' is other than H, to a subject in need thereof.

2. A method according to claim 1, in which the compound of the formula I is either:

(i) Formula Ia



Ia

5 in which:

R, R¹ and R³ are as defined in claim 1; and

R²ₐ is H; optionally substituted C₁-₆ alkyl; optionally substituted C₁-₆ alkenyl;

optionally substituted aryl; optionally substituted heterocyclyl; an antioxidant; a targeting moiety; COR⁶ₐ or CSR⁶ₐ in which R⁶ₐ is H, optionally substituted C₁-₆ alkyl, optionally

10 substituted C₂-₆ alkenyl, hydroxy, optionally substituted aryl, optionally substituted heterocyclyl or OR⁷ₐ, SR⁷ₐ or NR⁷ₐR⁸ₐ in which R⁷ₐ and R⁸ₐ are either the same or different and selected from

H, optionally substituted C₁-₆ alkyl, optionally substituted C₂-₆ alkenyl, optionally substituted aryl or optionally substituted heterocyclyl; CN; CH₂NR⁹ₐR¹⁰ₐ, HCNOR⁹ₐ or HCNNR⁹ₐR¹⁰ₐ in which R⁹ₐ and R¹⁰ₐ are either the same or different and selected from H, optionally substituted

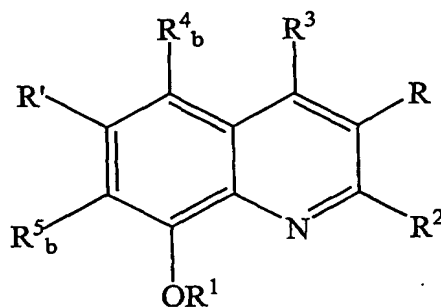
15 C₁-₆ alkyl, optionally substituted C₂-₆ alkenyl, optionally substituted aryl or optionally substituted heterocyclyl; OR¹¹ₐ, SR¹¹ₐ or NR¹¹ₐR¹²ₐ in which R¹¹ₐ and R¹²ₐ are either the same or different and selected from H, optionally substituted C₁-₆ alkyl, optionally substituted C₂-₆

alkenyl, optionally substituted aryl or optionally substituted heterocyclyl or together form optionally substituted heterocyclyl; or SO₂NR¹³ₐR¹⁴ₐ in which R¹³ₐ and R¹⁴ₐ are either the same

20 or different and selected from H or optionally substituted C₁-₆ alkyl, optionally substituted C₂-₆ alkenyl, optionally substituted aryl or optionally substituted heterocyclyl; or

- 120 -

## (ii) Formula Ib



Ib

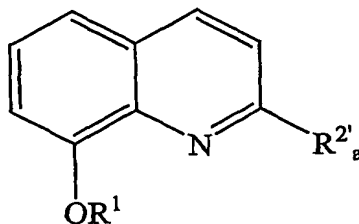
in which:

$R^1$ ,  $R'$ ,  $R$ ,  $R^2$  and  $R^3$  are as defined in claim 1;

$R^4_b$  and  $R^5_b$  are either the same or different and selected from H; optionally substituted  $C_{1-6}$  alkyl; optionally substituted  $C_{2-6}$  alkenyl; halo; CN;  $CF_3$ ; optionally substituted aryl; optionally substituted heterocyclyl; an antioxidant; a targeting moiety;  $SO_3H$ ;  $SO_2NR^{13}_aR^{14}_a$  in which  $R^{13}_a$  and  $R^{14}_a$  are as defined in formula Ia above; or  $OR^{15}_b$ ,  $SR^{15}_b$ ,  $SO_2R^{15}_b$ ,  $CONR^{15}_bR^{16}_b$  or  $NR^{15}_bR^{16}_b$  in which  $R^{15}_b$  and  $R^{16}_b$  are either the same or different and selected from H, optionally substituted  $C_{1-6}$  alkyl, optionally substituted  $C_{2-6}$  alkenyl, optionally substituted  $C_{1-6}$  acyl, optionally substituted aryl or optionally substituted heterocyclyl, including provisos (a) to (c), (e), (g), (h), (I), (k), (o), (q), (r), and (u) as defined in claim 1.

3. A method according to claim 2, in which the compound of formula Ia is as follows:

○ Formula IIa



IIa

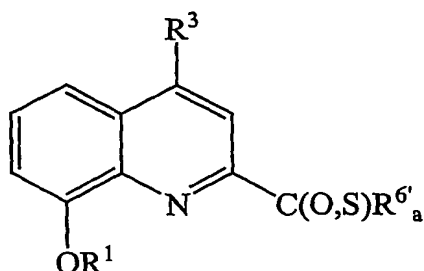
in which:

$R^1$  is as defined in claim 1 or claim 2; and

$R^{2'}_a$  is optionally substituted  $C_{1-6}$  alkyl, optionally substituted  $C_{2-6}$  alkenyl,

optionally substituted aryl or optionally substituted heterocyclyl;

o Formula IIIa



IIIa

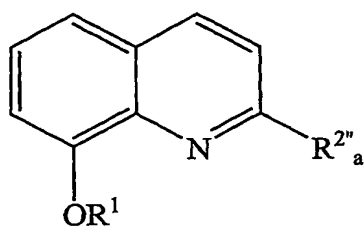
5 in which:

R¹ and R³ are as defined in claim 1 or claim 2; and

R⁶' is optionally substituted C<sub>1-6</sub> alkyl, optionally substituted C<sub>2-6</sub> alkenyl, hydroxy, OR<sup>7'</sup><sub>a</sub>, SR<sup>7'</sup><sub>a</sub>, N<sub>2</sub>R<sup>7'</sup><sub>a</sub>R<sup>8'</sup><sub>a</sub>, or NR<sup>7'</sup><sub>a</sub>R<sup>8'</sup><sub>a</sub> in which R<sup>7'</sup><sub>a</sub> and R<sup>8'</sup><sub>a</sub> are either the same or different and selected from H, optionally substituted C<sub>1-6</sub> alkyl, optionally substituted aryl or optionally substituted heterocyclyl;

10

o Formula IVa



IVa

in which:

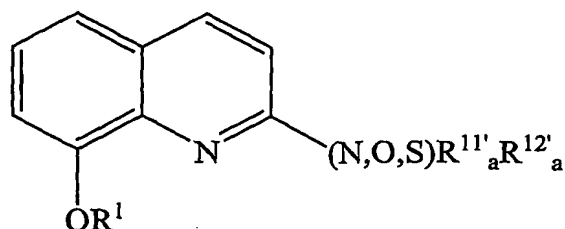
R¹ is as defined in claim 1 or claim 2; and

R²'' is CN; CH<sub>2</sub>NR<sup>9'</sup><sub>a</sub>R<sup>10'</sup><sub>a</sub>, HCNOR<sup>9'</sup><sub>a</sub> or HCNNR<sup>9'</sup><sub>a</sub>R<sup>10'</sup><sub>a</sub> in which R<sup>9'</sup><sub>a</sub> and R<sup>10'</sup><sub>a</sub> are either the same or different and selected from H, optionally substituted C<sub>1-6</sub> alkyl, optionally substituted alkenyl, optionally substituted aryl or optionally substituted heterocyclyl;

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- 122 -

o Formula Va

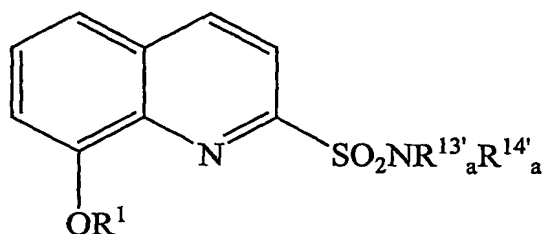


Va

in which:

- 5           R¹ is as defined in claim 1 or claim 2; and  
             R¹¹'ₐ and R¹²'ₐ are either the same or different and selected from H, optionally  
 substituted C₁-₆ alkyl, optionally substituted C₂-₆ alkenyl, optionally substituted aryl and  
 optionally substituted heterocyclyl or together form optionally substituted heterocyclyl; or

10           o Formula VIa



VIa

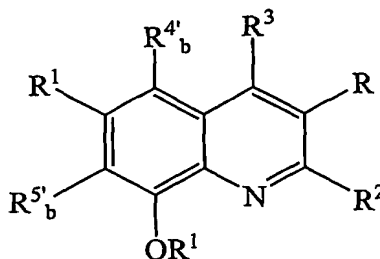
in which:

- R¹ is as defined in claim 1 or claim 2; and  
             R¹³'ₐ and R¹⁴'ₐ are either the same or different and selected from H, optionally  
 15   substituted C₁-₆ alkyl, optionally substituted C₂-₆ alkenyl, optionally substituted aryl or  
 optionally substituted heterocyclyl.

- 123 -

4. A method according to claim 2, in which the compound of the formula Ib is as follows:

• Formula IIb



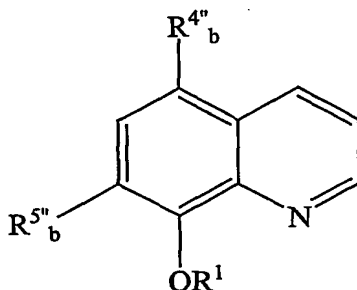
IIb

5 in which:

$R^1$ ,  $R'$ ,  $R$ ,  $R^2$  and  $R^3$  are as defined in claim 1 or claim 2; and

$R^{4'}$  and  $R^{5'}$  are as defined in formula Ib above provided that at least one is halo, including provisos (a), (c), (g), (h), (i), (o), (q) and (u) defined in claim 1;

10 • Formula IIIb



IIIb

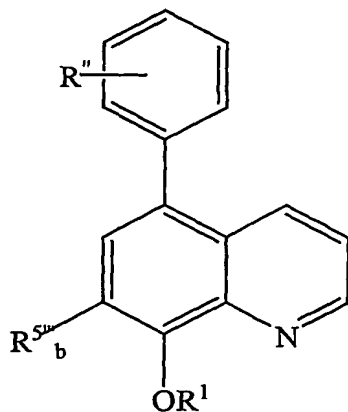
15 in which:

$R^1$  is as defined in claim 1 or claim 2;

$R^{4''}$  is H or halo; and

$R^{5''}$  is optionally substituted aryl or optionally substituted heterocyclyl;

- Formula IVb



IVb

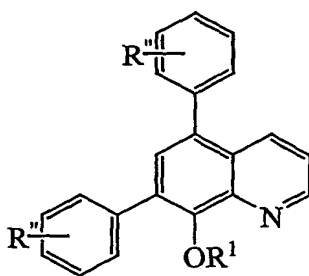
in which:

$R^1$  is as defined in claim 1 or claim 2;

$R''$  is  $C_{1-6}$  alkoxy, halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl or  $C_{1-6}$  haloalkyl; and

$R^{5b}$  is H or halo;

- Formula Vb



Vb

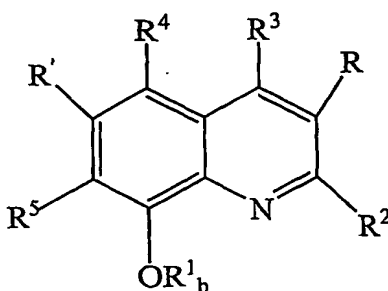
in which

$R^1$  is as defined in claim 1 or claim 2; and

$R''$  is as defined in formula IVb above; or

- 125 -

o Formula VIb



VIb

in which:

$R^2$  to  $R^5$ , R and R' are as defined in claim 1 or claim 2; and

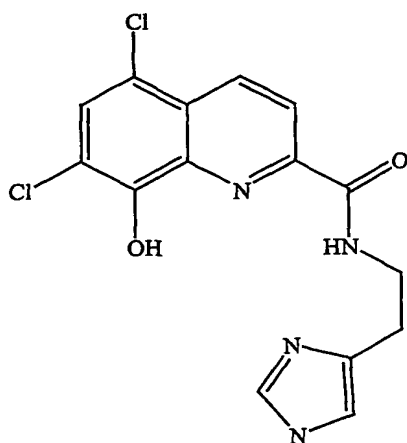
$R^1_b$  is optionally substituted  $C_{1-6}$  alkyl, optionally substituted aryl, optionally substituted aryl acyl,  $C_{1-6}$  alkyl acyl or optionally substituted heterocyclyl.

5. A method according to any one of claims 1, 2 or 4, in which the compound of formula I is a compound of formula Ib or IIb in which  $R^4_b$  and  $R^5_b$  or  $R^4_{b'}$  and  $R^5_{b'}$  are both halo.

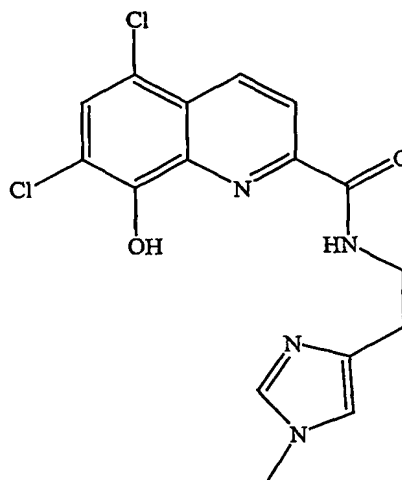
6. A method according to claim 5, in which the halo is chloro.

10 7. A method according to any one of claims 1, 2 or 4 to 6, in which at least one of  $R^2$ , R,  $R^3$  and R' is optionally substituted alkyl, optionally substituted aryl, optionally substituted heterocyclyl,  $CH_2NR^9R^{10}$  in which  $R^9$  and  $R^{10}$  are as defined in claim 1,  $COR^6$  in which  $R^6$  is  $NR^7R^8$  in which  $R^7$  and  $R^8$  are as defined in claim 1 or  $NR^{11}R^{12}$  in which  $R^{11}$  and  $R^{12}$  are as defined in claim 1.

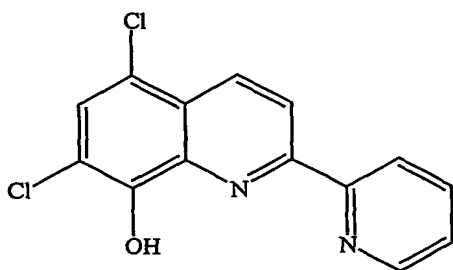
15 8. A method according to any one of claims 1, 2 or 4 to 7, in which the compound of formula I is as follows:



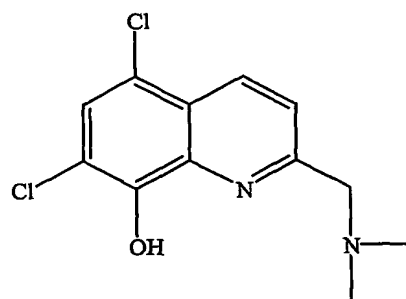
PBT 1038



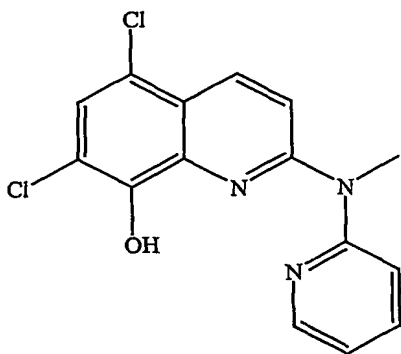
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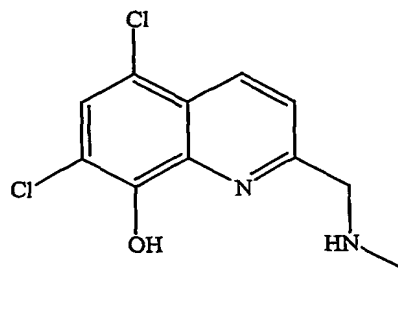
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PBT 1033



PBT 1056



PBT 1051

9. A method according to any one of claims 1 to 8, in which the neurological condition is a neurodegenerative disorder.

10. A method according to claim 9, in which the neurodegenerative disorder is

5 neurodegenerative amyloidosis.

11. A method according to claim 9 or claim 10, in which the neurodegenerative disorder is sporadic or familial Alzheimer's disease, amyotrophic lateral sclerosis, cataract, Parkinson's disease, Creutzfeldt-Jacob disease and its new variant associated with "mad cow" disease, Huntington's disease, dementia with Lewy body formation, multiple system atrophy,  
5 Hallerboden-Spatz disease, diffuse Lewy body disease, fatal familial insomnia, Gertsman Straussler Sheinker disease or hereditary cerebral haemorrhage with amyloidosis-Dutch type.

12. A method according to claim 11, in which the neurodegenerative disorder is Parkinson's disease.

13. A method according to any one of claims 9 to 11, in which the neurodegenerative  
10 disorder is an A $\beta$ -related condition.

14. A method according to claim 13, in which the A $\beta$ -related condition is Alzheimer's disease or dementia associated with Down syndrome or one of several forms of autosomal dominant forms of familial Alzheimer's disease.

15. A method according to any one of the preceding claims which slows, reduces or  
15 arrests the cognitive decline of the subject.

16. A method according to any one of the preceding claims, which further comprises separate, sequential or simultaneous administration of another medicament.

17. A method according to claim 16, in which the other medicament is an inhibitor of the acetylcholinesterase active site, an antioxidant, an anti-inflammatory agent or an oestrogenic  
20 agent.

18. A method according to any one of the preceding claims, in which the compound of formula I is administered orally, topically or parenterally.

19. Use of the compound of formula I as defined in any one of claims 1 to 8, in the manufacture of a medicament for the treatment, amelioration and/or prophylaxis of a  
25 neurological condition.

20. Use of a compound of formula I as defined in any one of claims 1 to 8 for the treatment, amelioration and/or prophylaxis of a neurological condition.

21. A compound of formula I as defined in claims 1 to 8 for use in the treatment, amelioration and/or prophylaxis of a neurological condition.

30 22. Use of the compound of formula I as defined in any one of claims 1 to 8, as a pharmaceutical.

23. Use according to 22, in which the pharmaceutical is a neurotherapeutic or neuroprotective agent.

24. Use according to claim 22 or claim 23, in which the pharmaceutical is an  
35 anti-amyloidogenic agent.

25. A pharmaceutical or veterinary composition comprising the compound of formula I as defined above in any one of claims 1 to 8 and a pharmaceutically or veterinarily



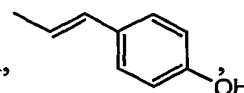
acceptable carrier.

26. A composition according to claim 25 which further comprises another medicament.

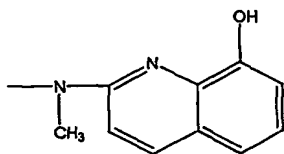
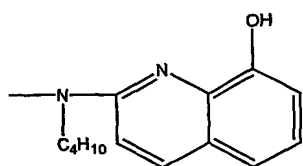
27. A composition according to claim 26, in which the other medicament is an inhibitor of the acetylcholinesterase active site, an antioxidant, an anti-inflammatory agent or an oestrogenic agent.

28. A compound of formula II which is a compound of formula I as defined in any one of claims 1 to 8, with the provisos that:

(a) when  $R^1$  and  $R^3$  to  $R^5$ ,  $R$  and  $R'$  are H, then  $R^2$  is not H, methyl,



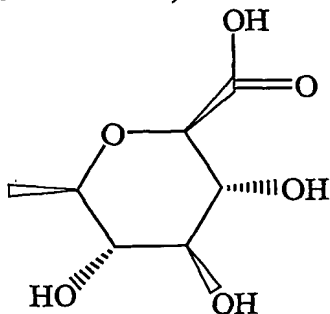
$\text{CO}_2\text{H}$ ,  $\text{CN}$ ,  $\text{CONCH}_2\text{CO}_2\text{H}$ ,  $\text{COCH}_3$ ,  $\text{CH}_2\text{NH}_2$ ,  $\text{CNOH}$ , (pyrid-2-yl), 2-hydroxyphenyl,  $\text{CHNHNH}_2$ ,  $\text{NH}(\text{pyrid-2-yl})$ ,



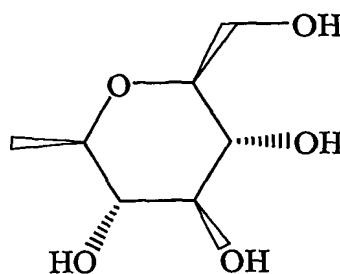
or  $\text{SO}_3\text{H}$ ;

(b) when  $R^1$  and  $R^4$  to  $R^7$  are H, then  $R^3$  is not OH and  $R^2$  is not  $\text{CO}_2\text{H}$ ;

(c) when  $R^1$  to  $R^3$ ,  $R^6$  and  $R^7$  are H, then (i) when  $R^5$  is I,  $R^4$  is not Cl,  $\text{SO}_3\text{H}$  or I; (ii) when  $R^5$  is H,  $R^4$  is not  $\text{SO}_3\text{H}$ ,  $\text{NH}_2$  or Cl; (iii)  $R^4$  and  $R^5$  are both not Cl, Br or  $\text{CH}_3$ ; and (iv) when  $R^2$  to  $R^7$  are H, then  $R^1$  is not

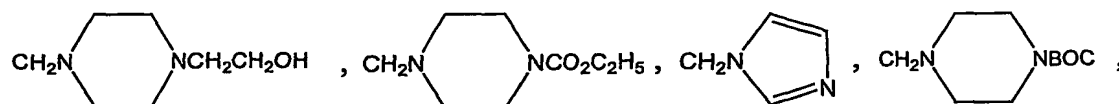
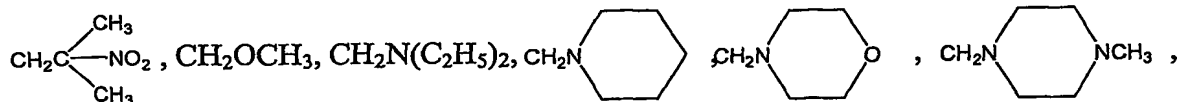


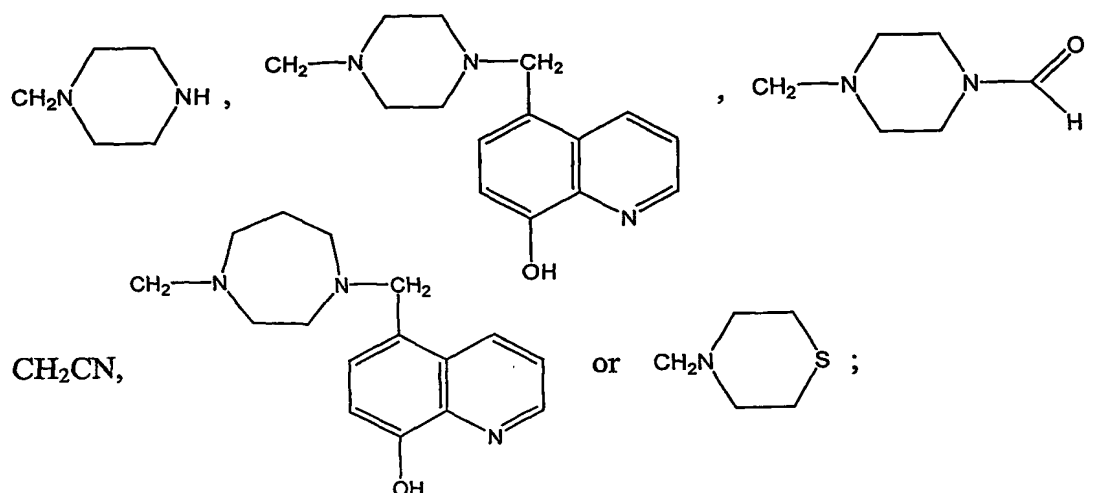
or



(d) when  $R^1$  to  $R^3$ ,  $R$  and  $R'$  are H, then  $R^4$  is not Cl or I and  $R^5$  is not I;

(e) when  $R^1$  to  $R^3$ ,  $R$ ,  $R'$  and  $R^5$  are H, then  $R^4$  is not CHO,  $\text{CHOHCCl}_3$ ,





- (f) when R<sup>1</sup>, R<sup>5</sup>, R' and R are H, R<sup>2</sup> is CO<sub>2</sub>H and R<sup>3</sup> is OH, then R<sup>4</sup> is not bromo, methyl, phenyl, hydroxymethyl or trifluoromethyl;
- (g) when R<sup>1</sup>, R<sup>4</sup>, R<sup>5</sup> and R are H, R<sup>2</sup> is CO<sub>2</sub>H and R<sup>3</sup> is OH, then R' is not bromo, iodo, methyl, phenyl, propyl, phenethyl, heptyl, benzylaminomethyl, 3-aminopropyl, 3-hydroxypropyl, 4-methoxyphenyl, 3-methylphenyl, 4-chlorophenyl, 3,4-dichlorophenyl, pyridin-3-yl, furo-2-yl, 4-chlorophenyl, 3,4-dichlorophenyl, 2-chlorophenyl, 3-chlorophenyl, 2-chlorophenyl, 3-chlorophenyl, 2-methoxyphenyl or piperidin-2-yl;
- (h) when R<sup>1</sup>, R<sup>4</sup>, R and R' are H, R<sup>2</sup> is CO<sub>2</sub>H and R<sup>3</sup> is OH, then R<sup>5</sup> is not phenyl, 3-hydroxypropyl, phenethyl, 3-aminoprop-1-yl or hex-1-yl;
- (i) when R<sup>1</sup>, R<sup>4</sup>, R' and R<sup>5</sup> are H, R<sup>2</sup> is CO<sub>2</sub>H and R<sup>3</sup> is OH, then R is not N-morpholinomethyl, bromo or phenyl;
- (j) when R<sup>1</sup>, R and R' are H, R<sup>2</sup> is CO<sub>2</sub>H and R<sup>3</sup> is OH, then R<sup>4</sup> and R<sup>5</sup> are not chloro;
- (k) when R<sup>1</sup>, R<sup>4</sup> and R' are H, R<sup>2</sup> is CO<sub>2</sub>H and R<sup>3</sup> is OH, then R and R<sup>5</sup> are not bromo;
- (l) when R<sup>1</sup>, R, R' and R<sup>5</sup> are H, R<sup>2</sup> is CO<sub>2</sub>Me and R<sup>3</sup> is OH, then R<sup>4</sup> is not hydroxymethyl, phenyl or bromo;
- (m) when R<sup>1</sup>, R, R<sup>4</sup> and R<sup>5</sup> are H, R<sup>2</sup> is CO<sub>2</sub>Me and R<sup>3</sup> is OH, then R' is not 4-methoxyphenyl, 3-methylphenyl, pyridin-3-yl, benzyl, bromo, 4-chlorophenyl, 3,4-dichlorophenyl, 3-hydroxypropyl or 3-tert-butoxycarbonylaminopropyl;
- (n) when R<sup>1</sup>, R, R<sup>4</sup> and R' are H, R<sup>2</sup> is CO<sub>2</sub>Me and R<sup>3</sup> is OH, then R<sup>5</sup> is not phenyl or 3-tert-butoxycarbonylaminoprop-1-yl;
- (o) when R<sup>1</sup>, R, R<sup>4</sup>, R' and R<sup>5</sup> are H and R<sup>2</sup> is CO<sub>2</sub>Me, then R<sup>3</sup> is not toluene-4-sulphonylamino, piperazin-1-yl, morpholin-1-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, 3-

- 130 -

benzoylaminoprop-1-yl, phenethyl, 3-tert-butoxycarbonylaminopropyl, 3-hydroxypropyl, amino or hex-1-yl;

(p) when  $R^1$ ,  $R^4$ ,  $R'$  and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Na}$  and  $R^3$  is OH, then R is not phenyl;

(q) when  $R^1$ ,  $R$ ,  $R^4$ ,  $R'$  and  $R^5$  are H and  $R^2$  is  $\text{CO}_2\text{H}$ , then  $R^3$  is not phenyl, 4-

5 chlorophenyl, phenethyl, 3-hydroxypropyl, amino, morpholin-1-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, toluene-4-sulphonylamino, 3-benzoylaminoprop-1-yl, aminoprop-1-ynyl, hex-1-yl, 5-hydroxypent-1-yl, piperazin-1-yl or 2-(1-piperazinyl)pyrimidinyl;

(r) when  $R^1$ ,  $R'$  and R are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then  $R^4$  and  $R^5$  are not chloro;

10 (s) when  $R^1$ ,  $R^4$ ,  $R'$  and  $R^5$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then R is not bromo;

(t) when  $R^1$ ,  $R'$  and  $R^4$  are H,  $R^2$  is  $\text{CO}_2\text{Me}$  and  $R^3$  is OH, then R and  $R^5$  are not bromo;

(u) when  $R^1$ ,  $R$ ,  $R^3$ ,  $R'$  and  $R^5$  are H and  $R^2$  is  $\text{CO}_2\text{H}$ , then  $R^4$  is not phenyl, 4-chlorophenyl or phenylethyl;

15 (v) when  $R^1$ ,  $R^5$ ,  $R'$ ,  $R^4$ ,  $R^3$  and R are H, then  $R^2$  is not 2H-tetrazol-1-yl;

(w) when  $R^1$ ,  $R^5$ ,  $R^4$  and R are H,  $R^2$  is  $\text{CO}_2\text{H}$  and  $R^3$  is OH, then  $R'$  is not 3,5-dichlorophenyl or 4-fluorophenyl; and

(x) at least one of  $R^1$  to  $R^5$ , R and  $R'$  is other than H;

(y) when  $R^1$  to  $R^3$ ,  $R^5$ ,  $R'$  and R are H, then  $R^4$  is not chloro,  $\text{NH}_2$  or  $\text{SO}_3\text{H}$ ; and

20 (z) when  $R^1$ ,  $R^3$  to  $R^5$ , R and  $R'$  are H, then  $R^2$  is not  $\text{CH}_3$ .

29. A process for the preparation of the compound of formula II defined in claim 28 as described herein.